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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/765,231	01/18/2001	Deborah J. Phippard	3221-US	7382

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EXAMINER	
CHEN, LIPING	
ART UNIT	PAPER NUMBER
1632	

DATE MAILED: 10/22/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/765,231	PHIPPARD ET AL.	
	Examiner	Art Unit	
	Liping Chen	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondenc addr ss --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 September 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-7,10-13,18,23-25,28,29 and 31* is/are pending in the application.

4a) Of the above claim(s) *31* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7,10-13,18,23-25,28 and 29* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☒ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Status of the claims

A restriction was made on 04/24/2002. Applicant's election without traverse of Group I, claims 1-7, 10-13, 18, 23-25, 28 and 29, in Paper No. 9, is acknowledged. Claims 1, 10, 11, 18, 23-25 and 29 are amended. Claims 8, 9, 14-17, 19-22, 26, 27 and 30 are cancelled from further consideration pursuant to 37 C.F.R. 1.142(b). Claim 31 is withdrawn as being to a non-elected invention

Claims 1-7, 10-13, 18, 23-25, 28, 29 and 31 are pending and Claims 1-7, 10-13, 18, 23-25, 28 and 29 are examined in this office action on the merits.

Priority

This application is filed on 01/18/2001.

Priority claimed to provisional application 60/176,523, filed 01/18/2000.

Oath/Declaration

It does not claim benefit of 60/176,523, filed on 01/18/2000.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 10 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 10, as written is indefinite as using the term "substantially identical to SEQ NO: 58". There is no concrete structure boundary as what percentage identity is substantially. The depending claims 12 and 13 are rejected to for being dependent on indefinite claim 10.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 2-7, 10-13, 18 and claim 23-25 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 2-4 are directed to nucleic acid capable of specifically hybridizing to the nucleic acid of claim 1; claims 5 and 7 are directed to any one of the nucleic acid

of claims 3 and 4, where the nucleic acid is detectably labeled, claim 6 is directed to the nucleic acid of claim 5 is a marker of osteoarthritis progression; Claim 10 is directed to a substantially purified nucleic acid having at least one 10 nucleotide region substantially identical to SEQ NO: 58; claim 11 is directed to a recombinant DNA comprising any one of nucleic acid of claims 2-4 and a promoter or partial promoter region, claim 12 is directed to a host cell containing a nucleic acid of claim 10, claim 13 is directed a method for producing and purifying a polypeptide by culturing the host cell of claim 12 under conditions suitable for the expression of the peptide; and recovering the polypeptide from the host culture; claim 18 is directed to a composition comprising a nucleic acid of any one of claim 2-3 and a complement thereof, claims 23-25 are directed to a substantially purified nucleic acid molecule which comprises a nucleic acid sequence that is identical to at least 10 nucleotides (claim 23), 50 nucleotides (claim 24), or 100 nucleotides (claim 25) of a nucleotide sequence selected from the group consisting of SEQ ID NO: 58, and a complement thereof.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111 (Fed. Cir. 1991), clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention.* The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" *Vas-Cath Inc. v. Mahurkar*, 19USPQ2d at 1117. The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she]

invented what is claimed." *Vas-Cath Inc. v. Mahurkar*, 19USPQ2d at 1116. In the instant case, while a written description for identifying initial expressed sequence tags (ESTs, page 10, line 19) by comparing three EST libraries of OA cartilage and synovium with two EST libraries from donors without OA and the derived sequence having SEQ ID NO:58 (specification, page 14, line 6-9) is generally understood, there is no written description regarding to how to define a specifically hybridizing to a nucleic acid of claim 1 is related with SEQ ID NO:58. Further there is no written description regarding how to define a nucleic acid exhibiting a percentage identity of between about 70% to about 90% with at least a 10 nucleotide region of the sequence of a nucleic acid of claim 2 is a SEQ ID NO:58 related nucleic acid, there is no definition as which 10 nucleotide region is necessary for identifying a nucleic acid is associated with instant invention, there is also no written description regarding the conserve nucleic acid is necessary for SEQ ID NO:58 so that all hybridized nucleic acid will be associated with the claimed sequence. Therefore a skilled artisan cannot envision all nucleic acids claimed. Therefore, with the exception of the SEQ ID NO: 58, the skilled artisan cannot envision the detailed chemical structure of any other nucleic acids claimed. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of identifying it. See *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016 (Fed. Cir. 1991). Possession may be shown by actual reduction to practice,

clear depiction of the invention in a detailed drawing, or by describing the invention with sufficient relevant identifying characteristics (as it relates to the claimed invention as a whole) such that a person skilled in the art would recognize that the inventor had possession of the claimed invention. *Pfaff v. Wells Electronics, Inc.,* 48 USPQ2d 1641, 1646 (1998).

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence. In the instant case, nucleic acid sequence of SEQ ID NO:58, but not the full breadth of the claim meets the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

Claims 1-7, 10-13, 18, 23-25, 28 and 29 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claim 1 is directed to a nucleic acid having nucleotide sequence selected from the group consisting of SEQ ID NO:58 and a complement thereof, claims 2-4 are

directed to nucleic acid capable of specifically hybridizing to the nucleic acid of claim 1, claims 5 and 7 are directed to any one of the nucleic acid of claims 3 and 4, where the nucleic acid is detectably labeled, claim 6 is directed to the nucleic acid of claim 5 is a marker of osteoarthritis progression; claims 10 and 23-25 are directed to different percentage homolous or complement or the nucleic acid of claim 1, claim 11 is directed to a recombinant DNA comprising any one of nucleic acid of claims 1-4 and a promoter or partial promoter region, claim 12 is directed to a host cell containing a nucleic acid of claim 10, claim 13 is directed a method for producing and purifying a polypeptide by culturing the host cell of claim 12 under conditions suitable for the expression of the peptide; and recovering the polypeptide from the host culture, claim 18 is directed to a composition comprising a nucleic acid of any one of claim 1-3 and a complement thereof, claims 23 is directed to a substantially purified nucleic acid molecule which comprises a nucleic acid sequence that is identical to at least 10 nucleotides of SEQ ID NO:58 or a complement, claim 28 is directed to a transformed cell having a nucleic acid molecule of claim 1, claim 29 is directed a transformed cell having the antisense of a nucleic acid molecule of claim 1.

The specification addresses that the instant invention identifies nucleic acid sequences and genes involved in the biology of osteoarthritis (OA) and represents targets from which diagnostic tools, such as monoclonal antibodies, can be generated to aid in monitoring treatment, definition and diagnosis of OA as well as

new targets for therapeutic drug invention (specification, page 3, line 1-5). The specification provides an example of identifying initial expressed sequence tags (ESTs, page 10, line 19) by comparing three EST libraries of OA cartilage and synovium with two EST libraries from donors without OA. The specification states that the identified ESTs are representative of genes upregulated as a result of OA (specification, page 71, line 9-16). Further, the specification states that the selected set of sequences represent a group of genes encoding multiple molecular targets for OA diagnostics (specification, page 14, line 12-14). However, the sequence search results under the claimed condition show many OA unrelated sequences meet the claimed conditions, such as GenBank accession number AAT69543, which is 100% identical to SEQ ID NO:58 in the nucleic acids 128-148 (pertaining to instant claims 10-13 and 23), which is related to metastasis (see attached sequence search report, RESULT 20), and SEQ ID NO: 58 shows 103 nucleic acid match with SE ID NO:2 of U.S. Patent 5,389,526 (pertaining to instant claims 23-25, see attached sequence search report, page , RESULT 1), which is a nucleotide sequence of the Dictyostelium plasmid Ddp2 ('526, col. 7, line 49-50). Since the claimed sequences can hybridize OA unrelated sequence, it is impossible to use the claimed sequences as molecular targets for OA diagnosis, because the increased expression level detected by hybridization may due to unrelated gene expression increased as a result of unrelated diseases. Further, it is well known in the art that polynucleotide sequence similarity does not correlate to the encoded protein structural similarity,

and that protein structural similarity does not reliably result in similar or identical biological function. A good example is a point mutation in a gene, such as a point mutation can result in the gene encoded protein disfunction as seen in the case of hemophilia B. It is found that point mutations in epidermal growth factor modules at amino acids which are Ca2+ ligands resulting in the biosynthesis of biologically inactive factor IX, (Stenflo et al. Biochim Biophys Acta 1477:51-63, 2000, Abstract). Therefore, SEQ ID NO:58 and a group of genes, which are derived from hybridization assay, encoding multiple molecula targets can not be OA diagnostics, or a marker of OA progression, and nucleic acid hybridization assay alone cannot diagnose OA.

Further, the specification addresses to use the selected sequence to detect protein structure and the activity (specification, page 15, line 14-29), screen for the homologue protein (specification, page 18, line 4-16) and protein identification (specification, page 21, line 7 to page 22, line 3). Attwood (Science, 290:471-473, 2000) teaches that the problem of predicting protein structure remains unsolved is because that we do not fully understand how the primary structure of a protein determines it tertiary structure. However, we must keep in mind that like sequences, structure alone will not inherently tell us function. Although the motifs may suggest roles of protein functionality, but such information does not reveal its specific biological function (Attwood, page 471, Figure, and page 472, right col. sec. and third parag.), which is involved in interrelated networks, such as gene

expression, metabolic pathways, and signaling cassades (Attwood, page 273, left col. sec. parag.). Although the specification suggests to express proteins identified by transforming different cells (specification, page 25, line 11 to page 26, line 16) for protein purification (specification, page 22, line 4-28) or antibody production (specification, page 23, line 12 to page 25, line 9). However, there is no direction what is the function of SEQ ID,NO:58 encoding protein and the identified protein by the method of nucleic acid hybridization or bioinformatics suggested by the specification. As discussed above, nucleotide similarity cannot represent the encoding protein function similarity. With regard to the information obtained from bioinformatics, Attwood (2000) teaches that current methods to predict genes in uncharacterized DNA are unreliable, it is presumptuous to make functional assignments merely on the basis of some degree of similarity between sequences; very few structures are known compared with the number of sequences and structure prediction methods are unreliable; the degree of automation that has been used of necessity, with its imperfect tools and protocols, has led to the accumulation of much database misinformation; and the terminology has been imprecise, muddying perceptions of what can realistically be achieved (Attwood, page 471, left col. sec. parag.). Information used to predict genes includes signals in the sequence, content statistics, and similarity to known genes. In a recent test of gene detection tools on part of the *Drosophila* genome, the majority of these "gene finders" identified 95% of coding nucleotides, but intron/exon structures were correctly

predicted for only about 40% of genes. The different methods failed to find between 5% and 95% of genes, and incorrectly identified up to 55% (Attwood, page 471, left col. Last parag.). Attwood further teaches that to date, more than 540,000 protein sequences have been deposited in the nonredundant database maintained by the National Center for Biotechnology Informaiton (NCBI), and millions of expressed sequence tags (ESTs), which are partial sequences of clones that are often error prone, are housed in public and proprietary repositories. These numbers will snowball with the fruition of further genome projects. By contract, the number of unique protein structures is still less than 2000 (Attwood, page 471, right col. First parag,). Attwood further points out that protein function is involved in interrelated networks, such as gene expression, metabolic pathways, and signaling cassades. Unraveling these networks and their interactions will be vital to our understanding of normal and pathologic cell development, and will help us create an integrated mapping between genotype and phenotype (Attwood, page 273, left col. sec. parag.) Since both hybridization and bioinformatics methods are not reliable for identifying proteins that are functional similar, the methods for characterization of each individual protein identified will be tremendously diverse. Since besides SEQ ID NO:58, the specification does not provide any information regarding the sequence encoding protein, no related protein function available, no related protein interrelated networks, such as gene expression, metabolic pathways, and signaling cassades available, no related OA phenotype available, it would be undue amount

experimentation without a predictable degree of success to achieve characterizing the SEQ ID NO:58 encoding protein using cells expressing the protein or cells containing an antisence of a nucleic acid molecule of SEQ ID NO:58, and characterizing all identified proteins for the protein functions and the roles played in OA for further usage of the protein or antibody or antisense sequences in OA diagnosis and treatment application. Without knowledge of the biological functions of the proteins encoded by claimed nucleotides, the skilled artisan will not know how to use the products. It is noted that case law requires that the disclosure of an application shall inform those skilled in the art how to use applicants' alleged discovery, not how to find out, how to use it, for themselves (see In re Gardner et al. 166 USPQ 138 (CCPA 1970). The specification only teaches what is intended to be done, but does not actually teach how to do that which is intended.

Based upon the nature of the invention, the state of the prior art, the unreliability in gene discovery and protein identification base on nucleotide hybridization and bioinformatics, lack of information regarding the functions of SEQ ID NO:58 encoding protein and all claimed peptides encoded by claimed nucleotides, lack of information regarding any specific phenotype related with any claimed nucleotide encoding protein, lack of direction or guidance as how to use any nucleotides claimed reliably, the claimed invention would have required one skilled in the art to engage in an undue amount of experimentation without a predictable degree of success to achieve any specific and the breath of the invention.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 10, 12 and 13 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Jacobs et al (WO98/45436 A2, published 10/15/1998), N-Geneseq Accession NO: AAV89253.

Claim 10 is directed to a substantially purified nucleic acid having at least one 10 nucleotide region substantially identical to SEQ NO: 58; claim 12 is directed to a host cell containing a nucleic acid of claim 10; claim 13 is directed a method for producing and purifying a polypeptide by culturing the host cell of claim 12 under conditions suitable for the expression of the peptide; and recovering the polypeptide from the host culture.

Jacobs et al. discloses a polynucleotide sequence encoding human secreted protein (Jacobs, Abstract) comprising at least one 10 nucleotide region substantially identical to SEQ ID NO:58 as show in the sequence search report the sequence is 100% identical to the region of nucleic acids 124-149 of SEQ ID NO:58, that is 23

contiguous nucleotides identical to a region of SEQ ID NO:58 (see attached sequence search result, ID: AAV89253). Jacobs et al. further teaches preparation of protein by culturing transformed host cells under culture conditions suitable to express the recombinant protein. The resulting expressed protein can be purified from such culture using known purification processes (Jacobs, page 59, 1-2, and 28-31). Thus, Jacobs et al. clearly anticipates the claimed invention.

Claims 10, 12 and 23-25 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Slade et al. (U.S. Patent No. 5,389,526, issued 02/14/1995).

Claim 10 is directed to a substantially purified nucleic acid having at least one 10 nucleotide region substantially identical to SEQ NO: 58; claim 12 is directed to a host cell containing a nucleic acid of claim 10; claims 23-25 are directed to a substantially purified nucleic acid molecule which comprises a nucleic acid sequence that is identical to at least 10 nucleotides (claim 23), 50 nucleotides (claim 24), or 100 nucleotides (claim 25) of a nucleotide sequence selected from the group consisting of SEQ ID NO: 58, and a complement thereof.

Slade et al. ('526) disclose a full nucleotide sequence of the Dictyostelium plasmid Ddp2 polynucleotide sequence ('526, col. 9, line 9-11, and SEQ ID NO: 2) having 103 nucleic acid identical to SEQ ID NO: 58 of instant invention (see attached sequence search result 1 of us-09-765-231a-58.std.rni). Ddp2 was purified ('526, col. 15, line 14-17) and sequenced using ATP radio-labelled with ^{35}S ('526, col.

14, line 51-52). Further, Slade et al. teaches construction of recombinant plasmid vector including a promoter, and the gene of interests ('526, col. 5, line 37-42) for transforming cells such as E.coli ('526, col. 15, line 19-20). Thus, Slade et al. clearly anticipated the claimed invention.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 2-5, 7, 10-12, 18 and 23-25 are rejected under 35 U.S.C. 103(a) over Strausberg, et al. (19 August 1997), GeneBank Accession NO: AA502552 in view of Maniatis (Molecular Cloning-A Laboratory Manual, 1989, sec edition).

Claim 2 is directed to a nucleic acid capable of specifically hybridizing to a nucleic acid of SEQ NO: 58, claim 3 is directed to a nucleic acid having 70-90% identity to the nucleic acid sequence of claim 2 and with at least a 10 contiguous nucleotides identical region, claim 4 is directed a nucleic acid having 90-99% identity to the nucleic acid sequence of claim 3, that is about 63-89.1% identity to the nucleic acid sequence of claim 2, and with at least a 10 contiguous nucleotides

identical region to the nucleic acid sequence of claim 3, claim 5 is directed to the nucleic acid of any one of claim 3 or 4, wherein the nucleic acid is detectably labeled, claim 7 is directed to the nucleic acid of claim 5 wherein said label is selected from the group consisting of redioactive, fluorescent, chemi-luminescent, and chromogenic agents, and magnetic particles; claims 10 and 23 are directed to a substantially purified nucleic acid having at least one 10 nucleotide region substantially identical to SEQ NO: 58, claim 11 is directed to a recombinant DNA comprising any one of nucleic acid of claims 1-4 and a promoter or partial promoter region, claim 12 is directed to a host cell containing a nucleic acid of claim 10, claim 18 is directed to a composition comprising a nucleic acid of any one of claim 1-3 and a complement thereof, claims 23 is directed to a substantially purified nucleic acid molecule which comprises a nucleic acid sequence that is identical to at least 10 nucleotides of SEQ ID NO:58 or a complement, claims 24 and 25 are increase the number of identity as to 50 nucleotides (claim 24) or 100 nucleotides (claim 25).

Strausberg et al. discloses polynucleotide sequence that shows 97% residue identity to SEQ ID NO:58 with 99.5% local sequence identical to SEQ ID NO:58 in the region of nucleic acids 19-225 with only one base pair mismatch at the position of 144 (pertaining to instant claims 2-4, see attached sequence search result, Genbank Accession No: AA502552). A cDNA library is prepared (see the sequence search report). Although, Strausberg et al. does not describe how the library is prepared. The common method for preparation for preparation of cDNA library is

done by operately linking each of all cDNA sequences in the library to a promoter (pertaining to instant claim 11, see Maniatis, Chapter 8, construction and analysis of cDNA libraries) and transforming the resulted constructs to host cells (pertaining to instant claim 12, see Maniatis, Chapter 8, Fig. 8.8). The sequence is performed by Washington University Genome Sequencing Center. Although Strausberg et al. does not describe how to sequence the disclosed nucleotide, it is well know in the art that sequencing can only be processed using substantially purified nucleic acid sequence (pertaining to instant claims 10 and 23-25) and be labeled radioactively or fluorescently (pertaining to instant claims 5 and 7, see Maniatis, Chapter 13). The disclosed sequence in any solution is a composition comprising any nucleic acid of claims 2 and 3. This sequence has been publicly available since the publication date (08/19/1997). Thus, Strausberg et al. clearly obviate the claimed invention.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Liping Chen, whose telephone number is (703) 305-4842. The examiner can normally be reached on Monday through Friday from 8:00 to 5:00 (Eastern Standard Time). Should the examiner be unavailable, inquiries should be directed to Deborah Reynolds, Supervisory Primary Examiner of Art Unit 1632, at (703) 305-4051. Any administrative or procedural questions should be directed to Pauline Farrier, Patent Analyst, at (703) 305-3550. Papers related to this application may be submitted to Group 1600 by facsimile

transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center number is (703) 308-8724.

Liping Chen, Ph.D.
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